

ECCO-ESGAR Guideline for Diagnostics in Inflammatory Bowel Disease

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Chapter 4: Scores for Inflammatory Bowel Disease

4.1 Clinical and endoscopic scoring systems in IBD

Statement 4.1. ECCO-ESGAR Diagnostics GL (2018)

Clinical indices are useful for standardizing disease activity. However, despite widespread use, no score has been validated in clinical practice [EL5]

4.1.1 Clinical and endoscopic scoring systems in ulcerative colitis

There are several scoring systems presently available to classify disease severity in ulcerative colitis (UC) within the multiple domains of disease activity, which aid objective assessment of disease and guide therapeutic and monitoring strategies [1,2]. Although somewhat limited by subjective definitions, their strength lies in the potential to monitor patient progress over time [1].

The **Simple Colitis Clinical Activity Index (SCCAI)** [2, 3] and the **Paediatric Ulcerative Colitis Activity Index (PUCAI)** [4] are reliable and responsive scores with clear definitions for clinical response and remission (see Tables). SCCAI scores range between 0 and 19 points and include nocturnal bowel movements and faecal urgency, which affect patient quality-of-life (QoL) [3]. An SCCAI score <2 indicates clinical remission and a decrease of >1.5 points from baseline correlates with patient-defined significant improvement [5].

The **Mayo Clinic Index** (Partial Mayo Clinic Index and endoscopic subscore) and **Ulcerative Colitis Disease Activity Index (UCDAI)** are a composite assessment of clinical symptoms (stool frequency and rectal bleeding) and endoscopic severity (Table x) [6, 7]. While these indices are not validated, the Mayo Clinic Index is easy to apply and has been used for assessing therapeutic endpoints in adult clinical trials [8]. Clinical improvement is defined as the reduction of baseline scores by ≥3 points and clinical remission as an overall score ≤2 (and no individual subscore >1) or UCDAI ≤1 [6-8]. A **Partial Mayo Score (PMS)** <1 indicates remission [1]. The PMS has been shown to correlate well with the full scoring system [9, 10].

The **Truelove and Witts Severity Index** was described in 1955 [11]. Its elements reflect levels of systemic toxicity and provide objective criteria for assessment of acute severe colitis, need for hospitalization, and corticosteroid therapy [2] (Table y). The **Lichtiger Index** is a

modification of the Truelove and Witts Index and was used in the cyclosporine trial for steroid-refractory UC [12].

The **Pouchitis Disease Activity Index** was developed to provide a standard definition of pouchitis, including histological subscores [13]. A Pouchitis Disease Activity Index score ≥ 7 indicates acute pouchitis and remission is defined as a score ≤ 2 including endoscopic subscores ≤ 1 (Supplementary Tables 1 to 6).

Statement 4.1.1. ECCO-ESGAR Diagnostics GL (2018)

Endoscopic scores in ulcerative colitis (UC) should be used for standardization of care [EL5]. The Mayo Clinic subscore (MCS) is accepted and extensively used and the UC endoscopic index of severity (UCEIS) and the UC colonoscopic index of severity (UCCIS) are formally validated [EL2]. The Pouchitis Disease Activity Index provides a standard definition of pouchitis [EL4]

Endoscopic scoring systems in ulcerative colitis

A plethora of UC endoscopic scoring systems has been developed over the years [1, 2, 14, 15]. These systems are also increasingly used in clinical practice to guide treatment decisions with the aim of achieving mucosal healing (MH) (Table 1) [16-19].

The first attempt to classify endoscopic UC severity was performed by Truelove and Witts [11]. Mucosal appearance is classified into the following three categories: (1) normal or near normal, (2) improved, or (3) no change or worse. This classification lacks well-defined endoscopic descriptors.

Baron et al. subsequently evaluated interobserver agreement using rigid sigmoidoscopy [20]. The degree of disease activity is based on a 4-point scale (0–3) mainly according to bleeding severity. The presence of ulceration is not taken into account. A **Baron score** ≤ 1 (0, normal mucosa; 1, abnormal mucosa but non-haemorrhagic) is defined as endoscopic remission. The Baron score has not been formally validated.

Feagan et al. described the **Modified Baron Score** (MBS) in a placebo-controlled trial [21, 22]. Endoscopic activity is categorized according to a 5-point scale (0–4).

The **Powell-Tuck index** (also known as St. Mark's index) [23] grades the severity of inflammation using a 3-point scale (0–2), focusing on mucosal bleeding as the predominant variable.

The **Sutherland index** (UC Disease Activity Index, UCDAI) [7] was developed during a placebo-controlled trial. Mucosal appearance is described on a 4-point scale (0–3) evaluating the following three endoscopic findings: (1) friability, (2) exudation, and (3) spontaneous haemorrhage.

The **Rachmilewitz Endoscopic Index** [24] was developed during a controlled trial. The index includes the following four variables: (1) vascular pattern, (2) granularity, (3) mucosal damage (mucus, fibrin, exudate, erosions, ulcers), and (4) bleeding. The cut-off for endoscopic remission is ≤ 4 points.

The endoscopic component of the **Mayo Clinic Score** (MCS) [6] assesses inflammation based on a 4-point scale (0–3) as follows: (0) normal, (1) erythema, decreased vascular pattern, mild friability, (2) marked erythema, absent vascular pattern, friability, erosions, and (3) ulceration, spontaneous bleeding. The MCS is most commonly used in clinical trials [8]. Clinical response is defined as reduction of baseline MCS scores by ≥ 3 points and a decrease of 30% from the baseline score with a decrease of at least 1 point on the rectal bleeding

subscale or an absolute rectal bleeding score of 0 or 1 [18]. Clinical remission is defined as an MCS ≤ 2 and no individual subscore > 1 . MH has been defined as a subscore of 0 to 1 [18]. Interobserver agreement can vary markedly [18]. For the MCS, the most inflamed part determines the overall score.

The **Modified Mayo Score** (MMES) divides the colon into five segments and the score for each segment is added to give a Modified Score [25], which is multiplied by the maximal extent of inflammation and divided by the number of segments with active inflammation to give the final MMES.

The **Ulcerative Colitis Endoscopic Index of Severity** (UCEIS) is a validated endoscopic index that was developed due to the wide interobserver variation. UCEIS grades three endoscopic findings in the most severely affected part of the colon, namely vascular pattern, bleeding, and erosions and ulcers. Initially developed as an 11-point score, UCEIS was simplified to an 8-point tool scoring erosions and ulcers (0–2), vascular pattern (0–2), and bleeding (1–4) with a satisfactory interobserver agreement (κ 0.5) [26]. Friability has been excluded from this index. The extent of disease is not relevant in this score. While this score appears more responsive to change following treatment than the MCS, UCEIS is still not extensively used due to lack of familiarity [27, 28]. The remission target is a score ≤ 1 . The UCEIS shows strong correlation with patient-reported outcomes [29–31]. Both UCEIS and MCS have demonstrated a high degree of correlation for UC (Supplementary Table 7) [32].

The **Ulcerative Colitis Colonoscopic Index of Severity** (UCCIS) has recently been prospectively validated [33]. The UCCIS includes the following six variables: (1) vascular pattern, (2) granularity, (3) ulceration, (4) bleeding and friability, (5) grading of segmental and global assessment of endoscopic severity with a predefined 4-point scale, and (6) global assessment of endoscopic severity on a 10-cm visual analogue scale (VAS) scale. While the UCCIS has good to excellent interobserver agreement, a cut-off level for endoscopic response and remission is currently lacking.

Supplementary Table 1. Clinical scoring system for the Simple Clinical Colitis Activity Index [3]

Symptom	Score
Bowel frequency (day)	
1–3	0
4–6	1
7–9	2
>9	3
Bowel frequency (night)	
1–3	1
4–6	2
Urgency of defecation	
Hurry	1
Immediately	2
Incontinence	3
Blood in stool	
Trace	1
Occasionally frank	2

Usually frank	3
General well being	
Very well	0
Slightly below par	1
Poor	2
Very poor	3
Terrible	4
Extracolonic features (joints, eyes, mouth, skin, perianal)	1 per manifestation

Supplementary Table 2. The Powell-Tuck (St Mark's) Index [23]

Symptoms and signs	Score
Bowel frequency	
3–6	1
>6	2
Stool consistency	
Formed	0
Semi-formed	1
Liquid	2
Abdominal pain	
Before/after bowel motions	1
Prolonged	2
Anorexia	1
Nausea/vomiting	1
General health	
Normal	0
Slightly impaired	1
Activities restricted	2
Unable to work	3
Extracolonic manifestations	
One/mild	1
More than one/severe	2
Abdominal tenderness	
Mild	1
Marked	2
Rebound	3
Body temperature (°C)	
<37.1	0
37.1–38	1
>38	2
Blood in stool	
Trace	1
More than trace	2
Sigmoidoscopy	
Non-haemorrhagic	0
Friable	1
Spontaneous bleed	2

Supplementary Table 3. Disease activity in ulcerative colitis, adapted from Truelove and Witts [11]

	Mild	Moderate 'between mild and severe'	Severe
Bloody stools/day	<4	4–6	≥6 <i>and</i>
Pulse	<90 bpm	≤90 bpm	>90 bpm <i>or</i>
Temperature	<37.5°C	≤37.8°C	>37.8°C <i>or</i>
Haemoglobin	>11.5 g/dL	≥10.5 g/dL	<10.5 g/dL <i>or</i>
ESR	<20 mm/hr	≤30 mm/hr	>30 mm/hr <i>or</i>
CRP	Normal	≤30 mg/L	>30 mg/L

Supplementary Table 4. Mayo score for ulcerative colitis [6]

Mayo index	0	1	2	3
Stool frequency	Normal	1–2/day >normal	3–4/day >normal	5/day >normal
Rectal bleeding	None	Streaks	Obvious	Mostly blood
Mucosa	Normal	Mild friability	Moderate friability	Spontaneous bleeding
Physician's global assessment	Normal	Mild	Moderate	Severe

Supplementary Table 5. Paediatric Ulcerative Colitis Activity Index [4]

Variable	Points
Abdominal pain	
Absent	0
Ignorable	5
Not able to be ignored	10
Rectal bleeding	
None	0
Small amount (<50%) of stools	10
Small amount with most stools	20
Large amount (>50%) of stools	30
Stool consistency	
Formed	0
Partially formed	5
Completely loose	10
Number of stools in 24 hours	
0–2	0
3–5	5
6–8	10
9+	15

Nocturnal stools	
No	0
Yes	10
Activity level	
No limitations	0
Occasional limitation	5
Severe restrictions	10

Supplementary Table 6. Pouchitis Disease Activity Index [13]

Variable	Score
Clinical	
Stool frequency (daily)	0–2 (usual post-operative frequency, 1–2 stools more than baseline, >3 stools more than baseline)
Rectal bleeding	0–1 (absent/rare, present daily)
Urgency	0–2 (absent, occasional, usual)
Fever	0–1 (absent, temperature >100.5F)
Endoscopy	1 point each (oedema, granularity, friability, decreased or absent vascular pattern, mucous exudates, ulceration)
Histology	1–3 (mild, moderate, or severe polymorphonuclear leukocyte infiltration)
	1–3 (<25%, 25–50%, >50% ulceration)
Pouchitis defined as total score ≥7 points. Remission is score ≤2 with endoscopic subscore ≤1	

Supplementary Table 7. The Ulcerative Colitis Endoscopic index of Severity [26]

Descriptor (score most severe lesions)	Likert scale anchor points	Definition
Vascular pattern	Normal [0] Patchy obliteration (1) Obliterated (2)	Normal vascular pattern with arborization of capillaries clearly defined, or with blurring or patchy loss of capillary margins
Bleeding	None (0) Mucosal (1) Luminal mild (2) Luminal moderate or severe (3)	No visible blood Some spots or streaks of coagulated blood on the surface of the mucosa ahead of the scope that can be washed away Some free liquid blood in the lumen Frank blood in the lumen ahead of endoscope or visible oozing from mucosa after washing intraluminal blood, or visible oozing from a haemorrhagic mucosa
Erosions and ulcers	None (0) Erosions (1) Superficial ulcer (2)	Normal mucosa, no visible erosions or ulcers Small (<5 mm) defects in the mucosa, of a white or yellow colour with a flat edge Larger (>5 mm) defects in the mucosa, which are discrete fibrin-covered ulcers when compared with

	Deep ulcer (3)	erosions, but remain superficial Deeper excavated defects in the mucosa with a slightly raised edge
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Table 1. Comparison of endoscopic scoring indexes in ulcerative colitis. Adapted from Annese V et al. [34].

Score	Endoscopic variables	Strengths	Weaknesses	Proposed Remission Score
Truelove and Witts [11] Sigmoidoscopic assessment	No endoscopic descriptor definitions	----	----	----
Baron Score [20]	Vascular pattern, friability, bleeding	Easy to calculate	Does not evaluate ulcers Subjective interpretation of friability and bleeding Poor interobserver agreement	0–1
Powell-Tuck index (St. Mark's Index) [23]	Bleeding (non-haemorrhagic vs. haemorrhagic mucosa)	-----	Only evaluates bleeding Subjective interpretation	Not defined
Sutherland Index [7]	Friability, exudation, spontaneous haemorrhage	-----	Does not evaluate ulcers Not accurate in discriminating between mild to moderate friability	0
Mayo Endoscopic Subscore [6]	Erythema, vascular pattern, friability, erosions, ulcers, bleeding	Easy to calculate Widely used in clinical trials	Not accurate in discriminating between mild to moderate friability	0–1
Rachmilewitz Index [24]	Vascular pattern, granularity, mucosal damage (mucus, fibrin, exudate, erosions, ulcers, bleeding)	Easy to calculate	Subjective interpretation of mucosal damage and bleeding	0–4
Modified Baron Score [21]	Vascular pattern, granularity, hyperaemia, friability, ulceration, bleeding	Easy to calculate Used in clinical trials	No discrimination between superficial and deep ulceration	0
UCEIS [26]	Vascular pattern, bleeding, erosions, and ulcers	Accurate for the assessment of disease severity Developed following rigorous methodology	Low agreement for normal appearance of the mucosa	Validated
UCCIS [33]	Vascular pattern, granularity, ulceration, bleeding, and friability	Accurate, easy scoring as based only on only four different parameters Developed and validated following rigorous methodology Covers the entire colon	Single-centre development, high expertise Broader validation needed	Validated
UCEIS, Ulcerative Colitis Endoscopic Index of Severity; UCCIS, Ulcerative Colitis Colonoscopic Index of Severity.				

4.1.2 Clinical and endoscopic scoring systems in Crohn's disease

Numerous tools are available for assessing disease activity in Crohn's disease (CD) patients [35]. The most commonly used clinical activity indices are the **Harvey-Bradshaw Index** (HBI), the **Crohn's Disease Activity Index** (CDAI), and the **Perianal Disease Activity Index** (PDAI) (Table x) [36]. Measuring clinical activity is important but no longer sufficient, and both CDAI and HBI are limited by subjective interpretation (Supplementary Table 8) [37, 38].

The CDAI [37] was developed by Best et al. in 1976. The CDAI consists of eight factors, each summed after adjustment with a weighting factor. Remission is defined as CDAI <150 and a value >450 represents severe disease. Most major research studies on medications in CD define response as decrease in CDAI of >70 points [39].

The CDAI system has some limitations. These include interobserver variability; relevant weight for scores of 'general wellbeing' and 'intensity of abdominal pain' items, which are subjective and reflect patients' perceptions of their disease; and the calculation of the CDAI is based on a diary completed by the patient for 7 days before evaluation. This requirement precludes the use of the CDAI in everyday practice. Furthermore, the CDAI is not accurate in patients with fistulizing or stenotic behaviour and it is not useful in patients with previous extensive ileocolonic resections or stoma. Currently, however, the CDAI is the most frequently used index for clinical trials [40].

The HBI was developed in 1980 as a simpler version of CDAI. The HBI consists of only clinical parameters; the first three items are scored from the previous day. These items include general well-being, abdominal pain, number of liquid stools per day, abdominal mass, and complications.

The HBI relies primarily on assessment of patient symptoms with scattered use of objective parameters. It correlates poorly with biological evidence of active disease, including endoscopic assessments and C-reactive protein levels. Furthermore, the HBI has the limitation of overestimating disease activity in the setting of concomitant functional bowel symptoms while underestimating disease in a subset of patients who may have subclinical stricturing or penetrating luminal complications [41].

Patients with CD who have an HBI score ≤ 3 are very likely to be in remission according to the CDAI. Patients with a score of 8 to 9 or higher are considered to have severe disease.

The **Crohn's Disease Digestive Damage Score** (the Lémann score) considers damage location, severity, extent, progression, and reversibility as measured by diagnostic imaging modalities and history of surgical resection (see chapter on cross-sectional imaging). The Lémann score is expected to represent a patient's disease course and to assess the effect of various medical therapies [42].

Irvine developed the PDAI [43]. Each of the five elements identified was graded on a 5-point Likert scale. Correlation between the PDAI (maximum 20 points) and the physician and patient global assessment is good. A more recent scoring system proposed by Pikarsky et

al. [44] attempts to predict the outcome following surgical intervention in patients with perianal CD.

Statement 4.1.2. ECCO-ESGAR Diagnostics GL (2018)

The Crohn's disease endoscopic index of severity (CDEIS) and the simple endoscopic score for Crohn's disease (SES-CD) are validated and reproducible scoring systems measuring luminal endoscopic activity [EL2]. There is no validated definition and score of mucosal healing (MH) in Crohn's disease (CD).

The severity of postoperative CD recurrence in the neo-terminal ileum should be stratified using the Rutgeerts score [EL2]

There are currently three endoscopic scoring systems for CD, namely the **Crohn's Disease Endoscopic Index of Severity (CDEIS)** [45], the **Simple Endoscopic Score for Crohn's Disease (SES-CD)** [46], and the **Rutgeerts** endoscopic grading scale for post-operative recurrence (Table 2 and Supplementary Table 9) [34, 47].

The CDEIS scores CD activity (from 0 to 44) in five bowel segments (terminal ileum, right colon, transverse, left colon and sigmoid, and rectum) and considers specific mucosal lesions (such as ulcers and stenosis) and extent of disease [45, 48, 49]. The CDEIS is complicated to use, requires training and experience in estimating the extent of ulcerated or diseased mucosal surfaces, and expertise in distinguishing deep from superficial ulcerations. The CDEIS is also time consuming. It has consequently not become routine in clinical practice and is used mainly in clinical trials.

The SES-CD was developed to simplify the CDEIS. The SES-CD includes four variables, each considered in five bowel segments (ulcer size, extent of ulcerated surface, extent of affected surface, and stenosis). Scores range from 0 to 6. The SES-CD correlates highly with CDEIS. Defining SES-CD cut-offs must take into account endoscopically meaningful changes [46, 50]. However, as the SES-CD do not define MH, this score is currently not really used in clinical practice.

Rutgeerts et al. developed a score for grading lesions in the neo-terminal ileum and anastomosis [47]. This score is considered the gold standard for establishing the prognosis in cases of postoperative recurrence; a score of 3 and 4 are validated cut-offs for predicting clinical relapse. The **Modified Rutgeerts Score** refers to a more refined definition of grade i2, which includes lesions confined to the ileocolonic anastomosis (i2a) or moderate lesions on the neo-terminal ileum (i2b) [51].

4.1.3 Capsule endoscopy scores

The **Capsule Endoscopy CD Activity Index (CECDAI or Niv score)** was validated in a multicentre prospective study of patients with isolated small-bowel CD [52]. The CECDAI evaluates the following three endoscopic parameters: inflammation (A, 0 to 5 points), extent of disease (B, 0 to 3 points), and strictures (C, 0 to 3 points), both for the proximal and distal

segments of the small bowel based on the transit time of the capsule (Supplementary Table 10).

The **Lewis score** assesses villous oedema, ulcers, and stenosis and classifies CD activity from mild to severe [53]. The small bowel is first divided into three equal parts (tertiles) based on capsule transit time from the first duodenal image to the first caecal image. For each tertile, a subscore is determined based on the extent and distribution of oedema and on the number, size, and distribution of ulcers. The Lewis score is the sum of the worst affected tertile plus the stenosis score (Supplementary Table 11).

These small-bowel capsule endoscopy scoring systems have been developed only recently, and their usefulness in clinical trials and clinical practice remains to be seen [48].

Supplementary Table 8. Non-endoscopic Crohn's disease activity indices in clinical practice

Activity Index	Acronym	Range and (remission) values	Comments for clinical practice
Clinical			
Crohn's Disease Activity Index [3]	CDAI	0–600 (<150)	Calculation based on a 7-day diary Difficulty in assessment of perianal disease activity
Harvey-Bradshaw Index [38]	HBI	0–50 (≤4)	Simple and more practical
Perianal Crohn's Disease Activity Index [43]	PDAI	0–19	Problematic fistula severity assessment

Supplementary Table 9. The most commonly used endoscopic scores for Crohn's disease

Score	Variables included	Field of applicability	Comments
Rutgeerts score [47]	Aphthous ulcers, ulcers, aphthoid ileitis, erythema, cobblestone, stenosis	Postoperative recurrence (only at the site of ileocaecal anastomosis)	Widely accepted, easy and suitable for routine practice, relevant prognostic value
Modified Rutgeerts score	Grade i2 lesions confined to ileocolonic anastomosis (i2a) or moderate lesions on the neo-terminal ileum (i2b)	Postoperative recurrence grade i2	No significant difference on the probability of clinical recurrence in i2a and i2b patients
CDEIS [51]	Ulcers and ulcerated areas or surfaces affected by disease, ulcerated or nonulcerated stenosis in all ileocolonic segments explored	Luminal Crohn's disease	Validated and used in several trials, sensitive to variations in endoscopic activity. Complex and time-consuming, not suitable for routine practice
SES-CD [45]	Ulcer size, surfaces affected by ulcers, surfaces affected by disease, type of bowel narrowing (all scored in all ileocolonic segments explored)	Luminal Crohn's disease	Simplification of some CDEIS variables, results may be linearly derived into CDEIS values Still complex and time-consuming

CDEIS, Crohn's disease endoscopic index of severity; SES-CD, simple endoscopic score for Crohn's disease

Supplementary Table 8. CECDAI (Niv score) for capsule endoscopy [52]

A. Inflammation score
0 = None
1 = Oedema/hyperaemia/denudation (mild to moderate)
2 = Oedema/hyperaemia/denudation (severe)
3 = Bleeding, exudate, aphthae, erosion, ulcer <0.5 cm
4 = Ulcer 0.5–2 cm, pseudopolyp
5 = Large ulcer >2 cm

B. Extent of disease score
0 = No disease
1 = Focal disease (single segment)
2 = Patchy disease (2–3 segments)
3 = Diffuse disease (>3 segments)

C. Stricture score
0 = None
1 = Single-passed
2 = Multiple-passed
3 = Obstruction (non-passage)
CECDAI = proximal (A1 × B1 + C1) + distal (A2 × B2 + C2)

Supplementary Table 91. Lewis score for capsule endoscopy [53]

	Number	Extent	Descriptors
Villous appearance (worst-affected tertile)	Normal – 0	≤10% – 8	Single – 1
	Oedematous – 1	11–50% – 12	Patchy – 14
		>50% – 20	Diffuse – 17
Ulcer (worst-affected tertile)	None – 0	≤10% – 5	<1/4 – 9
	Single – 3	11–50% – 10	1/4–1/2 – 12
		2–7 – 5	>50% – 15
	≥8 – 10		(percentage of the frame)

	Number	Extent	Descriptors
			occupied by the largest ulcer)
Stenosis (whole study)	None – 0	Nonulcerated – 2	Traversed – 7
	Single – 14	Ulcerated – 24	Not traversed – 10
	Multiple – 20		
Lewis score = tertile with highest score (result of oedema and ulcers) plus score of stenosis for the entire small bowel			

Table 2. Characteristics of the most commonly used scores to assess endoscopic activity in Crohn's disease

Score	Applicability	Variable	Grading	
Rutgeerts score [47]	Post-operative CD	i0	No lesions in neoterminal ileum	
		i1	≤5 aphthoid ulcers	
		i2 (modified to i2a, i2b)	>5 aphthoid ulcers with normal mucosa in between, skip areas with larger lesions, or lesions or ulcers (<1 cm) confined to ileocolonic anastomosis Lesions confined to the ileocolonic anastomosis (i2a) or moderate lesions on the neo-terminal ileum (i2b)	
		i3	Diffuse aphthous ileitis with extensively inflamed mucosa	
		i4	Diffuse inflammation with large ulcers, nodules, or stenosis (or both)	
CDEIS [51]	Luminal CD	Deep ulcers (in all explored segments)	Absent (0 points) Present (12 points)	
		Superficial ulcers (in all explored segments)	Absent (0 points) Present (6 points)	
		Surface disease involvement (in all explored segments)	0–10 (result of visual-analogue scale transformation representing a complete ileocolonic segment)	
		Surface ulcer involvement (in all explored segments)	0–10 (visual-analogue scale transformation representing a complete ileocolonic segment)	
		Ulcerated stenosis (anywhere)	Absent (0 points) Present (3 points)	
		Nonulcerated stenosis (anywhere)	Absent (0 points) Present (3 points)	
		SES-CD [45]	Luminal CD	Ulcers (in all explored segments)
Ulcerated surface (in all explored segments)	None (0 points) <10% of the segment (1 point) 10–30% of the segment (2 points) >30% of the segment (3 points)			
	Affected surface (in all explored segments)	None (0 points) <50% of the segment (1 point) 50–75% of the segment (2 points) >75% of the segment (3 points)		
		Narrowing (in all explored segments)		None (0 points) Single, passable by endoscope (1 point) Multiple, passable by endoscope (2 points) Not passable, frank stenosis (3 points)
CDEIS, Crohn's disease endoscopic index of severity; SES-CD, simple endoscopic score for Crohn's disease				

4.2 Histologic scoring systems in IBD

Statement 4.2. ECCO-ESGAR Diagnostics GL (2018)

A validated histological score should be used in clinical practice for UC [EL3].

There are no scores validated in clinical practice for CD [EL5]

The histological examination of endoscopic biopsies is not only a crucial element in the diagnostic workup but also in the evaluation of therapeutic effect and in identification of dysplasia [2, 54, 55]. The European Society of Pathology (ESP) and the European Crohn's and Colitis Organisation (ECCO) published a consensus document [56, 57].

Since the publication of these guidelines, significant recent literature on histological healing and new histological scoring systems have added to our understanding of the assessment of disease activity, influencing the paradigms around grading and assessment of disease activity [58, 59].

Histological remission in IBD

In UC, histologic remission should be defined as evidence of normalization of the bowel mucosa. Active disease is defined by the presence of neutrophils within the crypt epithelium and crypt lumen (cryptitis and crypt abscesses) and ultimately by erosions and ulcers [56, 57]. Histologically, MH is characterized by resolution of the crypt architectural distortion and of the inflammatory infiltrate [60], although the mucosa may still show some features of sustained damage, such as a decreased crypt density with branching and shortening of the crypts [61]. Ultimately, basal plasmacytosis decreases, resulting in normal cellularity and remission may result in a complete normalization of the mucosa in approximately 24% of cases [62, 63]. According to ECCO-ESP, active inflammation is usually absent in quiescent disease. There is no consensus on the number of eosinophils acceptable, lymphoid aggregates, or residual basal plasmacytosis. Although endoscopic MH is associated with better outcomes in IBD, less is known about the significance of achieving histological remission [64]. However, recent data suggest that histological remission, defined as minimal residual microscopic disease and absence of epithelial damage, is highly reproducible in multiple UC cohorts. Histological remitters are also more likely to achieve endoscopic and clinical response or remission and to remain symptom-free at 12 months after a course of corticosteroids. Reduced hospitalization or colectomy rates [65-68] have also been observed when histological remission is achieved.

There is a need for a clear definition of 'complete' histological MH, or 'histological remission' and to have a reproducible, standardized, and validated histological scoring system for biopsy evaluation.

A histological endpoint is likely to be more relevant in UC than CD, as the diffuse mucosal inflammation in UC is less subject to biopsy bias than the patchy transmural inflammation of CD.

Histological scoring systems

A unique standard system for grading histologic activity does not exist [69-71]. Numerous methods of classification of histologic activity have been proposed and some are widely used, with only a few validated and proven to be reproducible. Most the published systems were developed for UC. Bryant et al. [64] published the results of a systematic bibliographic search that retrieved 22 different histological scoring systems for IBD. The most widely used in UC are the Riley index [72] and the Geboes [73] index. Some (such as the Riley index) are difficult to reproduce, as the criteria for separating grades are not provided. While the Geboes index is also subjective for chronic inflammation (grade 1) and eosinophils and neutrophils in the lamina propria (grade 2), acute inflammation is well defined. The Geboes index also includes the requisites to grade architecture and can be modified to include the evaluation of basal plasmacytosis. The recently published Nancy score [59], a three-descriptor histological index, has been validated for use in clinical practice and clinical trials. The relationship between the Nancy score and Geboes index was assessed with good responsiveness and correlation between them [73]. Mosli et al. recently developed an alternative instrument using some component items of the Geboes index (Supplementary Table 12) [74].

Few scores were designed specifically for CD. The **Colonic and Ileal Global Histologic Disease Activity Score** (CGHAS or IGHAS) is probably the most widely used. This system is subjective and has not been validated and its role is currently undefined (Supplementary Table 13).

Practice points and future directions

There is a clear need for a standard definition of histologic MH and for a standard and fully validated system of histologic disease activity. Histology may be more effective in predicting clinical relapses or in evaluating benefit from therapy [37]. Meanwhile, pathologists should use a simple and validated scoring system to complement endoscopic scores. At present, the Nancy score and Robarts histopathology index are fully validated; the Geboes index is only partially (not formally) validated but is widely used.

Supplementary Table 10. Histological scoring systems in ulcerative colitis

Author	Description	Comments	Year of publication
Truelove and Richards [75]	3 grades	Subjective Partially validated	1956
Matts et al. [76]	5-grade scale: (1) normal to (5) ulceration, erosion, or necrosis of the mucosa	Not validated	1961
Watts et al. [77]	4-grade scale: (0) normal to (3) severe inflammatory changes	Not validated	1966
Korelitz et al. [78]	Mucosal cell counting in addition to histologic features	Not validated	1976
Powell-Tuck et al. [79]	3-grade scale: (1) no inflammation (2) mild inflammation (3) moderate-to-severe inflammation	Not validated	1982
Keren et al. [80]	Dichotomized: active versus inactive inflammation	Not validated	1984
Friedman et al. [81]	4-grade scale: (0) normal (1) lamina propria inflammation (2) crypt injury (3) ulceration	Not validated	1986
Gomes et al. [82]	5-grade scale: (0) normal to (4) severe inflammation and active ulceration	Not validated	1986
Saverymuttu et al. [83]	4 histological features: (1) enterocyte damage (2) crypt abnormalities (3) lamina propria involvement (4) acute inflammatory infiltrate in the lamina propria. Each graded from (0) normal to (3) severe.	Not validated	1986
Florén et al. [84]	Inflammatory response graded on a scale of 1–5	Not validated	1987
Riley et al. [72]	6 features graded 0–4	Simple but subjective grading system Reproducible Partially validated	1991
Hanauer S et al. [85]	4-point categoric scale	Used in the context of a trial, subjective	1993
Sandborn et al. [86]	4-grade scale: (0) inactive chronic colitis to (3) severely active chronic colitis	Not validated	1993
Hanauer SB et al. [87]	Scores active and chronic inflammation and crypt distortion; total score derived from the sum of the 3	Used in the context of a trial	1998
Geboes et al. [73]	6-grade classification system for inflammation, with subgrades	Reproducible grading system	2000

		Partially (not formally) validated	
Rutter et al. [19]	5-grade scale: (0) normal to (4) severe active inflammation	Not validated	2004
Rubin et al. [66]	6-grade scale: (0) normal to (6) crypt abscesses in >50% of crypts or presence of erosion or ulceration	Not validated	2007
Gupta et al. [88]	Harpaz score, 4-grade scale: (0) no cryptitis, (1) cryptitis <50% crypts, (2) cryptitis >50% crypts, or (4) ulcerations or erosions	Partially validated	2007
Nancy score [59]	5-level classification ranging from grade 0 (absence of significant histological disease activity) to grade 4 (severely active disease)	Correlation between the Nancy index and the Geboes index is very good Validated for use in clinical practice No predictive value data on outcomes in ulcerative colitis	2015
Robarts histopathology index Mosli et al. [74]	Based on Geboes index and modified Riley index	Robarts is a new validated histopathological index (compared with endoscopic and quality-of-life indices) with favourable operating properties No predictive value data on outcomes in ulcerative colitis	2017

Supplementary Table 13. Histological scoring systems in Crohn's disease

Author	Description	Comments	Year of publication
D'Haens et al. ^[89]	Developed for Crohn's Disease 16-point grading system 8 histological and distribution features	Subjective Not validated	1998
Baars et al. [90]	4-grade scale: (0) no active disease to (4) severe inflammation (numerous crypt abscesses)	Not validated	2012

4.3 Cross-sectional imaging scoring systems in IBD

Statement 4.3. ECCO-ESGAR Diagnostics GL (2018)

MR enterography-based indexes have high accuracy for assessing luminal CD activity and can be used in clinical trials for measuring activity and response to pharmacological interventions [EL3]. There are no validated scores for grading luminal activity based on ultrasound and CT enterography.

Scoring of perianal fistula activity by MRI in CD allows evaluation of disease severity and changes after therapy [EL3]

Cross-sectional imaging has an established role in clinical practice for evaluation of the small and large bowel in patients with CD [91]. Assessments based on cross-sectional imaging may have use in clinical trials with the added potential for validated indices as surrogates for therapeutic response.

Cross-sectional index for luminal Crohn's disease

There are no formally validated indexes on luminal activity based on ultrasonography or CT enterography. Among the different indexes published based on MR enterography, only a few have been derived using valid external reference standards (i.e. endoscopy or histology) and use descriptors identified in multivariate analyses as independent predictors for detecting activity and severity (Table 3) [92].

The **Magnetic Resonance Index of Activity** (MaRIA) is a composite index that takes into account bowel wall thickness, quantifies bowel enhancement after gadolinium injection, and identifies ulceration and bowel oedema. A subscore is calculated for five colonic segments and for the terminal ileum. The global score is computed as the sum total of the subscores. The MaRIA score has good correlation with CDEIS ($r=0.83$) [93, 94]. A MaRIA subscore of ≥ 7 is indicative of bowel segments with active CD and a subscore of ≥ 11 units identifies segments with severe activity (ulcers at endoscopy).

In a study by Takenaka et al., single-balloon enteroscopy was compared with MR enterography in patients with ileal CD [95]. The MaRIA score closely correlated with the SES-CD in the small bowel ($r=0.808$; $P<0.001$). A MaRIA score of ≥ 11 had high sensitivity, specificity, and diagnostic accuracy for ulcerative lesions (sensitivity, 78.3%; specificity, 98.0%). Similarly, a MaRIA score of ≥ 7 had high sensitivity, specificity, and diagnostic accuracy for all mucosal lesions (sensitivity, 87.0%; specificity, 86.0%).

The main limitation of the MaRIA index is that it was developed using both oral contrast and active colonic distension with water enema. It is still uncertain if diagnostic accuracy will remain similar without colonic distension [93]. MaRIA showed high accuracy for detecting ulcer healing (accuracy 0.9) and MH (accuracy 0.83) in CD patients following medical therapeutic intervention [96, 97].

The **Acute Inflammation Score** (AIS) is another MR enterography index and is a composite of two descriptors (mural thickness and mural T2 signal) that are evaluated in a semiquantitative fashion. A cut-off of 4.1 units defines the presence of active disease with an AUC of 0.77 and demonstrated a moderate degree of correlation with histopathological inflammation (Kendall's tau=0.40) [98].

Comparative studies using ileocolonoscopy as the reference standard have validated both indices [99, 100]. Reproducibility is critical to be considered as a useful instrument in practice. Specifically, moderate-to-good degrees of interobserver agreement (0.42–0.69) among expert readers has been reported (Supplementary Table 14) [99].

A recent index very similar to MaRIA but using diffusion-weighted imaging (DWI) sequence instead of contrast enhancement has been recently developed. This index is called the **DWI-MaRIA** score or **Clermont score** [101]. To derive and validate the DWI-MaRIA score, the same MR enterography (MaRIA) was considered as the reference standard [102]. The correlation between the MaRIA and Clermont score in the terminal ileum was almost perfect ($r=0.99$) but was significantly lower in the colon [103].

The **Sailer index** was developed specifically for assessing postoperative recurrence at the anastomotic site using MR enteroclysis [104, 105].

The most frequently used MRI index for perianal disease is the **Van Assche index** [106]. This score combines both the anatomical and complexity of fistula characteristics together with MRI findings linked to the inflammation observed. Changes in the Van Assche index have good correlation with clinical response to treatment [106-108]. This index has only been partially validated [109, 110]. However, certain aspects of the index need to be elucidated further, such as the responsiveness of each individual item of the index and the definition of a clinically relevant change in score [111].

Bowel damage index

The real potential for acute and chronic inflammation to cause bowel destruction through fibrosis and penetrating disease led the development of scoring systems for bowel damage [112]. The Lémann index was designed to measure damage severity in all segments of the digestive tract based on the assessment of stricturing and penetrating lesions using MR or CT and endoscopy together with previous surgery (Table 4). After an initial study [113], further studies demonstrated that up to 60% of patients had a reduction in score 1 year after starting anti-TNF therapy [114-116].

In conclusion, there are different available indices for grading luminal disease using MR enterography. MaRIA is the best-characterized among these indices. For perianal disease, there is need for an improved validated index for measuring response that overcomes the current limitations.

Table 3. Comparison of different MR enterography scoring systems

	Derived	Validated	Responsiveness	Reproducibility	Strengths	Limitations
MaRIA index [103, 117]	Ileocolonoscopy	Ileocolonoscopy	Yes (ileocolonoscopy)	Yes	Categorical classification in inactive, active, severe	Time consuming
AIS [118]	Histopathology	Ileocolonoscopy	No	Yes	Simplicity	No definition of severe lesions
DWI-MaRIA Clermont [101]	MR enterography (MaRIA)	MR enterography (MaRIA)	No	No	Categorical classification in inactive, active, severe	Controversial applicability of DWI sequence in large multicentre trials

MaRIA, Magnetic Resonance Index of Activity; AIS, Acute Inflammation Score; DWI-MaRIA, diffusion-weighted imaging MaRIA

Supplementary Table 11. Validation of MaRIA Score

Context of Use/Characterization	Publication	Comments/Evidence
MR enterography and definition of score and patient selection	Rimola et al. 2009 [103]	Derivation of the MaRIA score highly correlated with CDEIS and endoscopy
	Rimola et al. 2011 [117]	Verification of MaRIA correlation with endoscopy in an independent cohort
	Takenaka et al. 2015 [95]	High concordance between MaRIA and SES-CD; MaRIA accurate at detecting inflammatory activity in small bowel proximal to terminal ileum
Therapeutic response assessment	Ordas et al. 2014 [96]	Concordance between MR enterography and endoscopy assessment of response to anti-TNF with corticosteroids
Technical feasibility in multicentre setting	Coimbra et al. 2015 (FINCH) [93]	Multicentre feasibility and test-retest
Reproducibility	Tielbeek et al. 2013 [99]	Interreader reliability
	Coimbra et al. 2015 [93]	Test-retest, intrareader and interreader reliability

Supplementary Table 15. Lémann Index for the assessment of damage severity

Grade	Stricturing lesions (0–3)	Penetrating lesions (0–3)	Surgery
Null	Normal	Normal	Normal
Mild	Wall thickening <3 mm without pre-stenotic dilatation	–	-
Moderate	Wall thickening ≥3 mm without pre-stenotic dilatation	Transmural fissure with increased density in perienteric fat	Bypass strictureplasty
Severe	Stricture with pre-stenotic dilatation	Abscess or fistula	Resection
For each segment, severity of damage was scored on an ordinal scale ranging from 0 (normal) to 3 (maximal) for stricturing lesions and penetrating lesions.			

4.4 Quality-of-life scoring systems for IBD

Statement 4.4. ECCO-ESGAR Diagnostics GL (2018)

The Inflammatory Bowel Diseases Questionnaire (IBDQ) is considered the gold standard for use in clinical trials but is lengthy and thus impractical in clinical practice [EL3]. At present, there is insufficient evidence to recommend a specific quality-of-life (QoL) score in clinical practice [EL5]

Due to the wider appreciation that the nature of IBD has an often negative impact on patient's lives, emphasis on health-related quality of life (HRQoL) and its assessment are integral to the holistic care of patients with IBD [119, 120]. QoL is now a key measure in clinical trials in IBD [121]. This corresponds to the WHO statement that 'health is not merely an absence of disease' but rather 'complete physical, mental and social well-being' [122], which underpins the importance of improving HRQoL as a treatment objective [123].

HRQoL in IBD may be an indirect indicator of disease activity [124, 125] and an outcome measure when assessing the efficacy of treatment. There is reasonable expectation that effective treatment should improve QoL [126].

However, QoL is just one report from patients [1] in a continuum with general QoL measures on one end [127], disease (IBD)-specific HRQoL measurements [128] in the centre, and instruments that measure specific variables like continence [129], sexual dysfunction [130], food-related QoL [131], fatigue [132], and disability [133] on the other end. Some are specific for IBD whilst others can be used across all medical fields [121]. Disease-specific measures may be more sensitive to variable disease activity [134], whereas generic QoL instruments permit comparison of different patient populations [1, 135]. These instruments are not only used in adults and children alike, but the process has also been extended to parents [136-138], families, and carers [124].

The **Inflammatory Bowel Diseases Questionnaire** (IBDQ) is the foremost [128] and the most widely used tool. The IBDQ has up to 36 items and has been purported to represent the gold standard [139]. Short questionnaires may be more appropriate when time for completion is limited. In contrast, in the research setting, the need for more information may necessitate the use of longer questionnaires or even a combination of generic and disease-specific questionnaires [121, 134, 135, 140].

Two recent systematic reviews [120, 141] analysed IBD-specific tools. Another review has highlighted the fragmented approach to the use of QoL in this population [135]. Some of the limitations are summarized in Table 4.

The **Short Health Scale** (SHS) deserves a mention as it is only four questions. Developed in Sweden, the SHS showed good reliability, validity, and responsiveness in both patients with UC and CD [142, 143]. Some questions exist about its retest reliability [144]. English [142], Danish, and Korean versions have been also developed [143]. Additionally, the scale has been studied in children with IBD [145]. However, the SHS showed similar properties in patients with irritable bowel syndrome, thus indicating that this scale is a more generic and not a disease-specific instrument [146].

Table 4. Difficulties and limitations of extrapolation of data and study conclusions from published studies to real-world IBD patients [128]

Disease duration	A shorter history of IBD might have a greater impact on HRQoL (especially in the first year), whereas patients with long history might have encountered completely different treatment and diagnostic approaches
Disease phenotype	Extent and disease location has a variable impact on HRQoL
Gender distribution	Females consistently show lower HRQoL, which creates difficulties in comparing results across genders
Variability of IBDQ itself	The number of questions in IBDQ can vary from 30 to 36, the Likert scales can have between 4 to 7 points, and either 4 or 5 dimensions have been described, rendering comparison of different studies invalid.

The **Short-Form 36** health survey (SF-36) is the generic instrument for IBD patients [147, 148] and is used for both clinical and research purposes [134]. The SF-36 has eight dimensions, which are combined into two summary scores that reflect physical and mental components. Individual domain scores should be reported to allow comparison across different nationalities [135].

The **EQ-5D** is a shorter generic tool that has also been validated in IBD [149] but is less frequently used. The EQ-5D has five questions or domains that have the same set of answers and are combined with a standardized VAS.

As one instrument differs from another, the minimal clinically important change for each scale should be known (Supplementary Table 16).

Other instruments that assess a wider range of IBD-related issues not restricted to QoL are listed in Supplementary Table 17.

Supplementary Table 12. Suggested minimal clinically significant point changes in QoL measures

IBDQ [150]	16–30*
SF-36 (physical component) [151]	4.1
SF-36 (mental component) [152]	3.9
EQ-5D VAS [151]	9.2
*The original publication [128] states that a change between 16 and 30 points should be considered a meaningful difference, whereas later a fixed value of 16 points is used as the lowest meaningful change [153].	
IBDQ, Inflammatory Bowel Diseases Questionnaire; SF-36, Short-Form 36 health survey; VAS, Visual Analogue Scale.	

Supplementary Table 17. Other instruments not restricted to QoL

Abbreviation	Full title	Characteristics
RFIPC	Rating form of IBD patient concerns [154]	Measures worries and concerns of IBD – important psychosocial concomitants of the illness. With comparatively large number of publications [138], this instrument seems to have fallen out of favour and the last PubMed-indexed publication describing its use is dated 2012
SICC-IBD	Social Impact of Chronic Conditions– Inflammatory Bowel Disease questionnaire [155]	Measures the effect of disease on employment, family and social relationships, and personal independence
-	The IBD disability index [156]	Aims to measure the level of disability at social, family and work roles
CPWDQ	Crohn's Disease Perceived Work Disability Questionnaire [157]	
QUOTE-IBD	Quality of Care Through the Patient's Eyes with Inflammatory Bowel Disease [158]	A well-validated measure completed by patients to evaluate quality of care received
CCKNOW	The Crohn's and colitis knowledge score [159]	A 24-item tool to assess patient knowledge and understanding of their condition. Used and translated in multiple languages
KIDSCREEN	A HRQoL measure for children and adolescents with several variations that was developed simultaneously in 13 European countries [136]	Although not specific for IBD, it has been frequently used in studies on children and adolescents
IMPACT-III	A validated IBD-specific paediatric questionnaire [137]	Translated and used in multiple countries

Chapter 5 General principles and technical aspects of endoscopy including enteroscopy, capsule endoscopy, ultrasound, CT, MRI, and SBE/SBFT

5.1.1 Principles of conventional endoscopy

Sedation

Colonoscopy is generally perceived as unpleasant by patients. As stated by the European quality improvement initiative for lower gastrointestinal endoscopy, patient experience should be routinely measured and its improvement is crucial for acceptance [160]. Colonoscopy is an essential tool for diagnosing and monitoring IBD; biopsy and culture sampling is often needed. Although research on the development of different noninvasive surrogates is underway, current therapeutic goals include endoscopically assessed mucosal healing (MH). IBD patients undergo endoscopic procedures (mostly for surveillance) more often than the general population [161]. Hence, acceptance of the procedure is crucial for adequate management of the disease. Furthermore, endoscopy in IBD can be more demanding than in the general population; a prospective study on 558 colonoscopies in IBD patients showed a mean procedure time of 21 minutes. The current European quality initiative established a minimum standard of 6 minutes and a target standard mean of 10 minutes of withdrawal time [162]. A retrospective analysis of 5282 patients who underwent an outpatient colonoscopy associated the prior diagnosis of IBD with higher demand of sedation [163, 164]. Therefore, endoscopic procedures in IBD patients should be performed under deep sedation instead of conscious sedation or no sedation. Propofol-based sedation is currently the best option for deep sedation in most cases and should be administered by an endoscopist, anaesthesiologist, or trained nurse according to country-specific regulation [164-167]. Besides deep sedation, the use of CO₂ has been shown to improve patient comfort and satisfaction and should be implemented if possible [168].

Bowel preparation

Bowel preparation quality is important for the efficacy of colonoscopy and correlates with diagnostic yield and caecal intubation rate. Bowel preparation quality should be routinely measured according to validated scales [14, 160, 169]. Generally, patients with IBD do not have less successful bowel preparation outcomes but may have decreased preparation tolerance, which affects adherence. Regardless of the kind or the volume of the bowel preparation used, split-dose administration has demonstrated better quality and acceptance of the preparation in many studies. These results have been validated in two meta-analyses. Kilgore et al. included five trials and found that split-dose polyethylene glycol (PEG) was associated with satisfactory bowel cleansing and patient tolerability (odds ratio [OR] 3.7)[170]. Martel et al. obtained similar results in an analysis of 47 trials, including split dose of all available preparations (OR 2.5)[171]. Hence, split-dose administration of a low-volume PEG-based purgative should be recommended, especially in patients with previous preparation intolerance, intestinal hypomotility, or stenosis [169, 172-174]. Patients who have undergone many colonoscopies may have a personal preference for their bowel preparation that should be taken into consideration [169]. IBD could be considered as a relative contraindication for the use of sodium phosphate-based agents, which may also cause mucosal abnormalities that mimic IBD [169, 174].

Technical requirements and training

High-definition technology is preferred over standard colonoscopy, especially when performing dysplasia surveillance [14, 175]. Regardless of diagnostic or therapeutic intent, endoscopy in IBD is technically demanding and a thorough knowledge of the disease is also required. Moreover, some clinical scenarios (including severely active disease or endoscopic dilation) appear to be associated with higher risk of perforation [14].

To optimize diagnostic yield and impact of clinical management, IBD endoscopists should be experienced in both endoscopic and clinical management of the disease. Therefore, endoscopy in IBD should be considered as part of the specific training in IBD [176].

Statement 5.1.1. ECCO-ESGAR Diagnostics GL (2018)

Conventional endoscopy is essential for diagnosis and monitoring of IBD; patient experience and acceptance must be considered. Propofol-based deep sedation [EL5] and the use of CO₂ [EL5] should be offered. IBD endoscopy should be performed preferably by an endoscopist who is experienced in IBD endoscopy and also in IBD clinical management [EL5]. Bowel preparation with a split-dose polyethylene glycol (PEG)-based purgative is recommended [EL1]

5.1.2 Capsule endoscopy

Wireless video-capsule endoscopy is a method of endoluminal mucosal examination of the bowel. This form of endoscopy is based on a pill-sized camera tool that is swallowed by the patient and travels through the patients' luminal digestive tract through its intrinsic motor activity. The capsule continuously captures images that are wirelessly transmitted to a data recorder worn by the patient. Images are downloaded, processed, and examined by a trained gastroenterologist on a workstation.

Equipment

All currently available small bowel video capsules are appropriate for IBD [177]. Advances in technology have enabled wireless capsule endoscopy systems to examine the colonic mucosa. Despite substantial agreement shown in different endoscopic disease activity indices between capsule and conventional colonoscopy, there is insufficient data to recommend colon capsule studies in the evaluation of IBD [177, 178]. Recently, a new capsule endoscopy system has been developed that evaluates both the intestinal and colonic mucosa; data regarding its usefulness in IBD remains however scarce [179].

Patient preparation and basic technique

Patients should fast for at least 12 hours prior to capsule ingestion. The use of bowel preparation is recommended, as this has been shown to improve the visualization and the

diagnostic yield. Although there is not enough data to recommend any specific type of preparation, PEG in half dose (1 L), low volume (2 L), or high volume (4 L) has been shown to be beneficial [180]. As recommended for any other indication, following capsule ingestion with water, clear liquids may be taken after 2 hours and food and medications may be taken after 4 hours.

Appropriate documentation of the procedure and its findings in IBD patients undergoing capsule endoscopy should include standardized items. Use of IBD-specific scales such as the Lewis score and the capsule endoscopy Crohn's disease activity index are encouraged [53, 180, 181].

On the basis of a recent meta-analysis, the capsule retention rate in patients with suspected or known IBD is approximately between 4 and 8%. These rates decreased by half in studies that used either a patency capsule or a cross-sectional imaging technique (such as MR enterography or CT enterography) to assess patency before performing capsule endoscopy [182].

Training

Capsule endoscopy should be performed by a gastroenterologist experienced in conducting, interpreting, and reporting capsule endoscopy procedures [180]. Moreover, capsule endoscopy in IBD patients should be evaluated by gastroenterologists with experience in conventional endoscopy in IBD patients.

Statement 5.1.2. ECCO-ESGAR Diagnostics GL (2018)

Capsule endoscopy is appropriate to evaluate small-bowel Crohn's disease (CD). The use of bowel preparation [EL1] and simeticone [EL2] is recommended for capsule endoscopy

5.1.3 Enteroscopy

Equipment

Enteroscopy enables live assessment, treatment, and tissue sampling of the small bowel. Conventional push enteroscopy is intended to access only the proximal small bowel, but the median insertion typically does not exceed 100 cm from the angle of Treitz [183]. In patients with IBD, it may be necessary to reach deeper beyond the limits of ileocolonoscopy and push enteroscopy. Therefore, in IBD patients undergoing direct endoscopic assessment of the small bowel, device-assisted enteroscopy should be performed. There is not enough data to recommend any modality of device-assisted deep enteroscopy, either single, double-balloon, spiral enteroscopy, or balloon-guided endoscopy [184].

Patient preparation and basic technique

Fasting for at least 12 hours and avoidance of liquid consumption for 4 hours is generally sufficient for patients undergoing oral device-assisted enteroscopy. However, standard colonoscopy preparation is required for retrograde examination [185].

Device-assisted enteroscopy is clinically challenging and requires deep sedation or general anaesthesia. While this procedure seems to be as safe in IBD patients as in other populations, the general rate of major complications is estimated at 0.7%. Accordingly, this procedure should only be performed if indicated and change of clinical management is intended or expected [184, 186]. The use of CO₂ insufflation instead of room air is highly recommended in device-assisted enteroscopy procedures, as it may improve the intubation depth and reduce post-procedural discomfort [187, 188].

5.2. Small-bowel follow through and enteroclysis

Equipment

Small-bowel follow through (SBFT) and small-bowel enteroclysis (SBE) are performed using conventional X-ray equipment imaging. Digital fluoroscope technology is now widely available and allows real-time image projection and storage of image 'loops'. Digital technology facilitates better radiation dose control in the generally young IBD patient population. Equipment to compress, move, and separate the opacified small bowel should be available. SBFT and SBE have high accuracy for mucosal abnormalities (including ulcerations and strictures) and can possibly identify extramural complications, such as internal fistulae.

Patient preparation and basic technique

For both investigations, patients should be nil by mouth 6 hours prior to the procedure. SBFT may be augmented by pneumocolon to produce double-contrast imaging of the distal ileum, which enhances the sensitivity for detecting subtle mucosal changes [189]. Pneumocolon requires retrograde insufflation of gas (e.g. room air or CO₂) into the terminal ileum via a rectal tube and requires bowel preparation to remove intraluminal material prior to the procedure [190].

SBFT consists of oral administration of 400 to 600 ml barium sulfate suspension, typically 30 to 50% weight/volume over a specific period of time [191]. Ingested volumes should be individualized for each patient. This is followed by serial fluoroscopic interrogation of the small bowel and spot filming at intervals of 20 to 30 minutes, tracking passage of the contrast agent through the bowel. Targeted compression views of the small bowel are mandatory to ensure that the whole small bowel is visualized as far as possible. Magnified compression views also facilitate detailed evaluation of the small-bowel mucosa.

SBE requires placement of a nasojejunal catheter under fluoroscopic guidance and insufflating the small bowel with barium and air or methylcellulose to create a double-contrast distended view of the small bowel [192, 193]. Automated pump infusion is preferred over hand injection. SBE in general provides better distension of the small bowel than SBFT and has been suggested to improve evaluation of the bowel mucosa. However, any diagnostic superiority over SBFT remains unproven. Furthermore, conscious sedation is sometimes necessary due to the discomfort the procedure can cause.

Technical parameters

During SBE, infusion rates should be constantly adjusted to obtain uniform distention of the entire small intestine without overwhelming peristaltic capacity. All accessible segments of the small bowel should be manually or mechanically compressed during the course of infusion. This includes using rotation and palpation and special manoeuvres used to isolate pelvic small-bowel loops [191]. Large-format images should be obtained when the entire small bowel is adequately filled and distended. Similarly, segments of the small bowel should be manually or mechanically compressed to ensure adequate visualization during SBFT.

Barium sulfate is non-toxic and normally passed in stool. SBE is inherently more invasive, with tube placement under fluoroscopic guidance resulting in a higher radiation exposure than that from SBFT [194]. Although the radiation exposure for barium studies is lower than for CT, it is nevertheless a significant exposure for adults [195] and children [196], particularly when repeated examinations are performed. Moreover, excessive fluoroscopy time and frequent abdominal radiographs can result in doses that are equivalent to CT [196].

Training

SBFT and SBE are highly operator-dependent and patient radiation doses are influenced by the radiologist's technique [197, 198]. Consequently, dedicated gastrointestinal radiologists who are experienced in conducting and interpreting them should perform both procedures.

Statement 5.2.1. ECCO-ESGAR Diagnostics GL (2018)

Small-bowel follow through (SBFT) and small-bowel enteroclysis (SBE) have a diminishing role and are largely now replaced by cross-sectional techniques. However, they may have a role in specific clinical circumstances [EL5]

5.3 Cross-sectional imaging techniques

Reference should be made to the ESGAR/ESPR guidelines for the technical performance of cross-sectional small-bowel and colonic imaging [199].

5.3.1 MRI and CT

Equipment

MR enterography and MR enteroclysis should be performed at either 1.5T or 3T. No evidence supports the superiority of one platform over another [200, 201]. Phased-array coils should be used routinely. For perianal fistula MRI, phased-array surface coils are preferred to endocoils, given their larger field view and greater patient acceptance [202]. Due to the propulsive motor action of the gut, CT requires rapid acquisition of high-resolution images of the bowel. Although there are no comparative studies comparing different CT platforms, CT enterography and CT enteroclysis in general should be performed on scanners with at least 16 slices (ideally 64 or greater).

Patient preparation and basic technique

Patient preparation regimens are similar to MR enterography and CT enterography. Due to insufficient distension of the bowel, there is evidence that studies performed without oral contrast preparation have inferior diagnostic accuracy when compared with those performed after administration of oral contrast [203, 204]. Patients should be nil by mouth for solids for 4 to 6 hours prior to MR enterography or CT enterography. Liquids should also be restricted, although water is permissible. There are ranges of suitable oral agents available to distend the small bowel, usually with hyperosmolar properties [205]. These include mannitol, PEG, sorbitol, or combinations thereof [206-211]. There is currently no evidence that favours one preparation over another. Although use is not widespread, negative-contrast agents containing paramagnetic iron reduce luminal signal on both T1-weighted and T2-weighted images [212]. Oral contrast agents should be ingested 45 minutes prior to the examination [213]. Volumes over 1000 mL may give better distension [208], although it is possible to acquire diagnostically acceptable images with ingested volumes of 450 mL [214]. Patients should be warned that they might experience cramping and diarrhoea after ingesting hyperosmolar oral contrast agents. Enteroclysis is more invasive than enterography and is less well tolerated by patients [215] but may provide superior distension of the proximal small bowel in particular [216](59). MR enteroclysis and CT enteroclysis should be performed with similar distension agents as MR enterography and CT enterography, which should be infused via an 8F or 10F nasojejunal tube placed under fluoroscopic guidance. Automated pump infusion (at a rate of 80–120 ml/min) is preferred over hand injection, although both are acceptable. On-table monitoring of small-bowel distension should be performed during both MR enteroclysis and CT enteroclysis and infused volumes should be individualized for each patient [199].

Diagnostic accuracy for colonic inflammation is improved with colonic filling, either by prolonged oral contrast administration [217, 218] or via a rectal liquid enema [219]. However, additional colonic preparation is not required for routine MR enterography or CT enterography. While superior bowel distension may be achieved by placing the patient prone, there is no evidence that this translates into superior diagnostic accuracy over the supine position [220].

Technical parameters

CT images should be acquired following intravenous contrast agent administration in the enteric or portal venous phase only [221]. Iodinated contrast administration facilitates assessment of the bowel wall enhancement pattern and mesenteric vascularity. The use of multiplanar reformats is mandatory during CT evaluation and these should be reconstructed at 3 mm or less [222].

Radiation exposure is the major limiting factor for the use of CT in IBD [223, 224]. Exposure to high radiation doses can occur (primarily due to repeated CT) and particularly in those with young age of disease onset and complicated disease [225]. It is therefore imperative that dose

exposure is minimized by optimizing tube voltage and current [226, 227]. The use of automated tube current modulation reduces dose while maintaining image quality [228]. Furthermore, there is good data demonstrating that iterative reconstruction techniques significantly reduce dose while producing diagnostically acceptable images [229-233]; these techniques should be applied routinely when available. It is good practice to maintain a log of radiation exposure for patients with IBD undergoing repeat medical imaging [199]. Due to the risks from repeated radiation exposure given the chronic nature of the disease and need for repeated imaging, MRI is generally the preferred modality in IBD patients.

Although diagnostically acceptable MR enterography images can be acquired without use of spasmolytic agents [234], administration of these agents improves bowel distension [228] and use is currently recommended [199]. Hyoscine butylbromide (butylscopolamine) is the spasmolytic agent of choice, although glucagon is an acceptable alternative [235]. High-quality MR enterography and MR enteroclysis requires fast breath-hold sequences to minimize breathing and peristaltic artifacts. A typical protocol should include a combination of T2-weighted and steady-state free precession gradient echo (SSFP GE) sequences. T1-weighted images acquired in the enteric or portal venous phase following intravenous gadolinium contrast administration facilitates assessment of the bowel wall enhancement pattern and mesenteric vascularity, with some evidence that it increases diagnostic accuracy [236, 237]. However, recent studies have reported long-term retention of gadolinium in the brain of exposed patients [238-241], and protocols omitting gadolinium contrast may have similar diagnostic accuracy [242, 243]. Administration of gadolinium should therefore be considered on a case-by-case basis. There is increasing data supporting the use of diffusion-weighted imaging [243-246] and cine motility sequences [247-250] both in disease detection and activity assessment. Pending further research, these sequences are currently considered optional [199].

Sequence selection in perianal fistula imaging should include high-resolution T2-weighted images with and without fat saturation angled to the plane of the anal canal. Short T1 inversion recovery (STIR) sequences are an alternative to fat-saturated T2-weighted sequences [251, 252]. The use of gadolinium enhancement on T1-weighted imaging is useful for differentiating granulation tissue from fluid, for gauging fistula activity [107], and may increase staging accuracy [253].

Training

There is evidence of a learning curve in the interpretation of MR enterography. Initial data suggests that feedback on 100 cases is required to achieve diagnostic accuracy equivalent to experienced radiologists [254]. However, once trained, radiologists tend to maintain their interpretation skills long term [255]. Moderate-to-good interobserver agreement has been reported for MR enterography [99, 255, 256] and CT enterography [257], with one study suggesting higher reader agreement for CT enterography over MR enterography [258]. There are also data that confirmed a learning curve in the interpretation of MRI perianal fistula imaging, with improvement in accuracy after dedicated training [259].

Statement 5.3.1.1. ECCO-ESGAR Diagnostics GL (2018)

CT enterography and CT enteroclysis should be performed on CT scanners with at least 16 slices. MR enterography and MR enteroclysis can be performed at 1.5T or 3T [EL2]

Statement 5.3.1.2. ECCO-ESGAR Diagnostics GL (2018)

A suitable oral contrast agent should be administered 45 minutes prior to MRI and CT enterography or infused via nasojejunal tube prior to MR enteroclysis or CT enteroclysis [EL2]

Statement 5.3.1.3. ECCO-ESGAR Diagnostics GL (2018)

Dedicated colonic preparation is not part of routine protocols but can be achieved either by prolonged oral contrast or administration of a liquid rectal enema [EL2]

Statement 5.3.1.4. ECCO-ESGAR Diagnostics GL (2018)

Radiation exposure is a limitation of CT and should only be used if MRI or ultrasound is not available. Dose exposure must be minimized by optimizing acquisition parameters, use of tube current modulation, and iterative reconstruction techniques when available [EL2]. Cumulative radiation exposure of IBD patients should be monitored [EL5]

Statement 5.3.1.5. ECCO-ESGAR Diagnostics GL (2018)

MR enterography and MR enteroclysis should be performed with fast breath-hold sequences to minimize breathing and peristaltic artifacts [EL2]. Consideration should be made for the routine use of intravenous gadolinium in all patients, weighing the risks and benefits [EL4]

Statement 5.3.1.6. ECCO-ESGAR Diagnostics GL (2018)

Radiologists interpreting cross-sectional imaging in IBD require appropriate training, with initial evidence suggesting that radiologists should review at least 100 cases [EL2]

5.3.2 Ultrasonography

Equipment

Modern ultrasound devices have sufficient quality and screen resolution to delineate the structure of the gastrointestinal wall. The resolution of an ultrasound transducer is dependent on the frequency, the speed of sound in tissue, and the number of cycles in the ultrasound pulse. Since the thickness of the bowel wall layer is usually <3 mm [260], the frequency of the transducer must be at least 5 MHz for wall layers to be well discriminated. No head-to-head studies have been published comparing the diagnostic performance of regular low-frequency, mid-frequency, or high-frequency probes for detection of the normal small bowel and pathological findings. Harmonic imaging should be activated when available, as this may improve delineation of the bowel wall [261].

Doppler ultrasound can assess both blood flow in the visceral vessels that supply the gastrointestinal tract and the smaller vessels of the intestinal wall. Doppler ultrasound cannot

detect capillary flow. Colour Doppler or power Doppler can both be used to evaluate bowel wall vascularity [262]. Flow parameters should be optimized to maximize the sensitivity for the detection of vessels with low-velocity flow in the bowel wall. The information obtained from colour Doppler images is semi-quantitative. It is recommended to measure bowel wall vascularity according to the number of vessels detected per square centimetre [263-265]. Increased vascularity of the diseased bowel wall is a marker of disease activity. To improve the sensitivity of Doppler ultrasound, intravenous ultrasound contrast agents have been introduced. For example, the second-generation echo-signal enhancer SonoVue is injected as a bolus in units of 1.2 to 4.5 mL into an antecubital vein, immediately followed by injection of 10 mL of normal saline solution (0.9% NaCl) flush. For each examination, a recording is initiated a few seconds before the intravenous administration of the agent, and continuous imaging is performed for 40 seconds [266]. There are several ways of interpreting contrast enhancement in the bowel wall. These include pattern of enhancement [267, 268], contrast quantification at peak intensity [269], and dynamic contrast-enhanced ultrasound where intensity changes over time are analysed [270].

Contrast-enhanced ultrasound

Contrast-enhanced ultrasound (CEUS) can be used to quantify vascularity [271] but can also be used to separate vascular from avascular tissue, which is particularly useful when trying to differentiate a phlegmon from an abscess [272].

Small intestine contrast ultrasonography

In recent years, the use of oral contrast agents (such as PEG solution) has been introduced to distend the bowel for better characterization of the bowel wall and increased disease detection. The use of an oral contrast agent does not alter the procedure greatly; the same equipment is used with the addition of 375 to 800 mL of oral contrast fluid. However, the procedure duration increases, ranging from 25 to 60 minutes [273]. The accuracy for assessing lesions in the proximal small bowel and for defining the extent of diseased ileal walls can be significantly improved using small intestine contrast ultrasonography [274].

Ultrasound elastography

Gut fibrosis develops in up to 50% of Crohn's disease (CD) patients and is a major challenge [275]. Clinically suspected fibrostenotic disease is currently mainly investigated by contrast-enhanced CT [276] or MR [276, 277] enterography or MR enteroclysis or native ultrasound and CEUS (see above). Novel MRI sequences (such as magnetization transfer) also show promise [278, 279], although detection and characterization of fibrotic disease by imaging remains suboptimal. While MR elastography is being studied for staging several diseases (such as liver fibrosis), it has not been studied in fibrotic bowel disease. Ultrasound elasticity imaging based on strain under deformation and elastic modulus [280] is an evolving technique. Recent studies suggest that ultrasound elastography can differentiate between fibrotic and inflammatory stenosis independent of wall thickness and blood flow in CD [281, 282].

Patient preparation and basic technique

Abdominal ultrasound is most successful in nonobese patients due to its basic technical principle as discussed above. The small bowel and colon should be carefully and systematically interrogated, using gentle graded compression. No patient preparation is needed to perform bowel ultrasound. However, to reduce the amount of food and bowel gas, a fasting period of at least 4 to 6 hours is recommended, although there are no rigorous studies confirming this approach [283]. Administration of a spasmolytic agent is not required and indeed may interfere with the real-time assessment of bowel peristalsis by the operator. Colonic preparation or liquid enemas are also not required. As noted above, use of colour Doppler should be routine. While both CEUS and elastography are highly promising evolving techniques, they are not yet routinely used outside specialist centres.

Training

The interobserver agreement between operators with various degrees of experience in bowel ultrasound and its learning curve needs to be investigated further. Dedicated training in bowel ultrasound is necessary and should preferably be performed following training in general abdominal ultrasound [283, 284]. Preliminary data suggests that signs of CD in bowel ultrasound can be standardized and have shown fair-to-good reproducibility. In particular, bowel wall thickness shows excellent reproducibility [285].

Statement 5.3.2.1. ECCO-ESGAR Diagnostics GL (2018)

For a complete examination of the bowel with ultrasound, low-resolution and high-resolution probes should be used [EL5]

Statement 5.3.2.2. ECCO-ESGAR Diagnostics GL (2018)

The use of intraluminal orally administered contrast agents improves the overall accuracy in diagnosing small-bowel CD [EL2]

Statement 5.3.2.3. ECCO-ESGAR Diagnostics GL (2018)

Contrast-enhanced ultrasound (CEUS) of the bowel can be used to differentiate vascular from avascular intestinal or peri-intestinal lesions, including abscesses [EL3]

Statement 5.3.2.4. ECCO-ESGAR Diagnostics GL (2018)

A standard ultrasound examination of the intestine does not require specific patient preparation, although fasting is recommended before the examination [EL4]

Statement 5.3.2.5. ECCO-ESGAR Diagnostics GL (2018)

Dedicated training in bowel ultrasound is necessary and should be performed following training in general abdominal ultrasound [EL5]

CONFLICT OF INTEREST STATEMENT:

ECCO has diligently maintained a disclosure policy of potential conflicts of interests (CoI). The conflict of interest declaration is based on a form used by the International Committee of Medical Journal Editors (ICMJE). The CoI statement is not only stored at the ECCO Office and the editorial office of JCC but also open to public scrutiny on the ECCO website (<https://www.ecco-ibd.eu/about-ecco/ecco-disclosures.html>) providing a comprehensive overview of potential conflicts of interest of authors.

DISCLAIMER TEXT:

The ECCO Consensus Guidelines are based on an international Consensus process. Any treatment decisions are a matter for the individual clinician and should not be based exclusively on the content of the ECCO Consensus Guidelines. The European Crohn's and Colitis Organisation and/or any of its staff members and/or any consensus contributor may not be held liable for any information published in good faith in the ECCO Consensus Guidelines.

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WG1: Initial diagnosis (or suspecting IBD), Imaging techniques in regard to location: Upper GI tract, Mid GI tract, Lower GI tract, Perianal disease, Extraintestinal Manifestation

Leader – Stephan Vavricka
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WG2: Imaging techniques in regard to clinical situations: Monitoring therapeutic success (inclusive calpro), Monitoring clinically asymptomatic patients, Monitoring clinically symptomatic patients, Imaging after surgery including ileoanal pouch

Leader – Torsten Kucharzik
Member – Patrick van Rheenen
Member – Uri Kopylov
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WG3- Detecting (suspected) complications (stricture, fistula, abscess, anastomotic insufficiency, toxic megacolon, perforation): Endoscopic and non-medical, non-surgical interventions (stricture, abscess, bleeding), Cancer surveillance, Imaging during pregnancy

Leader – Gionata Fiorino
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WG4 : Endoscopic and clinical scoring systems in IBD: CDAI, CDEIS, Mayo-Score, Life quality indices, cross-sectional imaging

Leader – Vito Annese
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WG5: General principles and technical aspects of: endoscopy including enteroscopy, capsule endoscopy, ultrasound, CT, MRI, SBE/SBFT

Important note: The idea of your part is to help colleagues to set up standards at their institutions, e.g. what is mandatory for MR enteroclysis, requirements for endoscopy, ultrasonography, etc.

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SUPPLEMENTARY DATA

Supplementary data are available at ECCO-JCC online.

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